

A Study of Hyponatremia in Lower Respiratory Infections in Children Aged 2months to 5 Years.

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ABSTRACT

Background: We studied serum sodium levels within 2 hours of admission of 100 children aged 2months to 5 years admitted with diagnosis of lower respiratory infections(pneumonia,bronchiolitis, bronchitis, empyema and WALRI).

Methods: In our study out of these 100 cases 33(33%) cases were having hyponatremia (s.sodium<135mEq/L) & out of 33(33%) cases 17(51.5%) cases had mild hyponatremia i.e. s.sodium 131-134mEq/L, 14(42.5%) cases had moderate hyponatremia i.e. s.sodium 126-130mEq/L & 2(6%)cases had severe hyponatremia i.e. s.sodium <125mEq/L. These Children with hyponatremia were evaluated for plasma osmolality, urinary sodium and osmolality on day of admission and after appropriate fluid therapy. **Results:** Out of these 33 cases, the probable cause of hyponatremia was the syndrome of inappropriate secretion of antidiuretic hormone in 27(81.8%) cases (as suggested by their plasma osmolality,urinary sodium and urine osmolality). Symptoms and signs indicative of severe LRIs were about one and a half times more frequent and the mean duration of hospital stay was 49.2% longer in children with hyponatremia than with isonatremia. Two children (2%) with severe hyponatremia had complications in the form of convulsions associated with transitory altered sensorium for 2-3 days. The recovery from hyponatremia with timely intervention showed a good improvement in clinical symptomatology of respiratory distress and there was no mortality in the studied cases. **Conclusion:** Thus it is concluded that,presence of hyponatremia in LRI's increases the morbidity of these patients in the form of prolonged hospital stay and occurrence of complications like seizures followed by deranged sensorium in some cases.

Keywords: Lower Respiratory Infections, Hyponatremia, Sodium.

INTRODUCTION

Lower respiratory infection (LRI) is one of the serious illness especially in less than 5 year of age group requiring hospitalization and contributes to 30% of deaths yearly worldwide mainly due to pneumonia as the leading cause.^[1,2] These infections including pneumonia, empyema, bronchitis, bronchiolitis and WALRI continue to threaten the health of children worldwide, especially in developing countries.

Fluids and electrolytes are the main components in the maintenance of body homeostasis. The most

important being sodium which is the main cation of the extracellular fluids. Hyponatremia (s.sodium <135meq/L) is the most common electrolyte abnormality seen in intensive care unit (ICU) with an incidence as high as 30% in some reports.

In children lower respiratory tract infections, pneumonia and bronchiolitis are the most common diseases which are at particular risk of developing hyponatremia due to antidiuretic hormone(ADH) oversecretion.^[3-5] Hyponatremia associated with pediatric pneumonia is most commonly due to the syndrome of inappropriate secretion of antidiuretic hormone(SIADH). This syndrome is characterized by hyponatremia and hypoosmolality and results from the inappropriate and continued secretion and/or action of antidiuretic hormone despite normal or increased plasma volume.^[6] Sources of free water intake in these children include hypotonic intravenous fluids, gavage tube feeds and humidified air in the ventilator circuit.^[7] Acute hyponatremia in

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these patients can cause rapid shift of fluid in central nervous system causing brain oedema and their consequences.^[8]

Although hyponatremia is one of the most common electrolyte abnormality in children with LRI between 2months to 5 years of age, the number of research studies are limited. Therefore this study was conducted with the aim to know the incidence of hyponatremia in children with lower respiratory infections below 5 years to explore any relationship between hyponatremia and clinical outcomes of LRI including severity of LRI, duration of hospital stay and mortality.

MATERIALS AND METHODS

Study Design: this was a prospective study.

Study Site: BNMCCC, AMRITSAR (Pb), Department of pediatrics.

Study population: children aged 2months to 5 years admitted with a diagnosis of LRI.

Sample size:100

Selection of Cases: included inclusion and exclusion criteria as follows:-

Inclusion criteria:

1. Children between the age of 2months to 5 years with a diagnosis of LRI.
2. All children for whom consent was obtained from parents/guardian.

Exclusion criteria:

1. Infants <2 months of age.
2. Children > 5 years of age.
3. Children with associated gastroenteritis.
4. Children with associated renal disorders.
5. Children with associated CNS infection, congestive heart failure and adrenocortical disorders.
6. Those on drugs which can cause electrolyte imbalance such as diuretics, anticonvulsants.

Investigations:

Two venous samples were collected at the time of admission. The first urine sample was also collected. One venous sample was used for the estimation of serum sodium and serum potassium. The second serum sample and urine sample was refrigerated and were used for the work up for the diagnosis of SIADH, in those patients who had serum sodium value<135mEq/L. In these patients blood urea, serum creatinine, blood glucose, urinary sodium, urinary urea, urinary creatinine, urine osmolality & serum osmolality was estimated. X-ray chest was taken in all cases to confirm the diagnosis of lower respiratory infections. The patients' clinical data including age, sex, duration of hospital stay and the final outcome(discharge or death) were recorded in all the cases.

Normal Serum Sodium was taken as 135-145mEq/L. Serum Sodium concentration of <135mEq/L was

taken as hyponatremia. Serum Sodium concentration of 131-134mEq/L was taken as mild hyponatremia, 126-130mEq/L was taken as moderate hyponatremia and ≤ 125 mEq/L was taken as severe hyponatremia. Criteria for Diagnosis of SIADH in those patients with hyponatremia included.^[9]

- (1) Hyponatremia (S. $\text{Na}^+ < 135$ m Eq/L) together with decreased effective serum osmolality<280mOsm/kg.
- (2) Spontaneous urine osmolality>100mOsm/kg.
- (3) Spot urinary sodium concentration of >30mEq/L
- (4) Normal renal functions (blood urea and serum creatinine).

Collected data was analyzed statistically using SPSS software. p-value of <0.05 was considered as significant.

RESULTS

Results and observations were given after enrolling 100 children admitted with lower respiratory infections and after clinical, biochemical and radiological evaluation.

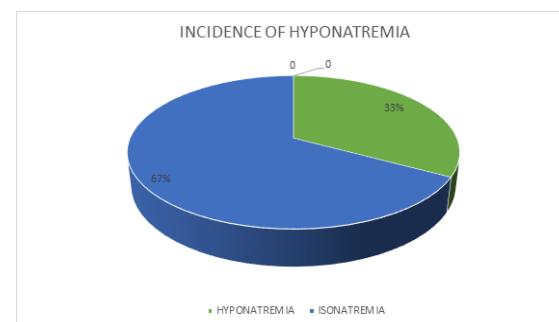


Table 1: Demographic Feature and Other Data of All Study Cases with lower Respiratory Infections

	Characteristics	Patients (n=100)	% age
Age	2 months – 1 year	75	75.0
	1-5 year	25	25.0
Sex	Male	70	70.0
	Female	30	30.0
Serum Sodium levels (in mEq/L) (Mean \pm SD)	Isonatremic	137.15 ± 2.84 mEq/L	
	hyponatremic	130.34 ± 3.47 mEq/L	
	Hyponatremia(n=100)	33	33.0
	Hyponatremia due to SIADH(n=33)	27	81.8
	No. of Patients with complication(n=33)	2	6.0

In this study of 100 children, majority belonged to 2months to 1 years (75%), whereas 25% belonged to 1-5 years of age group. Out of 100 children, 70 were male children (70%) and 30 were female children (30%). Out of 100 children, 33(33%) had hyponatremia. Out of 33 hyponatremic cases, 27(81.8%) were due to SIADH. Out of 33 hyponatremic cases, 2(6%) had complications in the form of seizures followed by altered sensorium.

Table 2: Age and sex wise distribution of study cases.

	Characteristics	Hyponatremia (n=33)	Normonatremia (n=67)
Age	2 months – 1 year	24 (72.7%)	51 (76.12%)
	1-5 year	9 (27.3%)	16 (23.88%)
Sex	Male (n=70)	23(69.7%)	47(70.25%)
	Female (n=30)	10(30.3%)	20(29.85%)

In 2-12 months age group, out of total 75 cases, hyponatremia was seen in 24(72.7%) cases while 51(76.12%) were isonatremic. In 1-5 year age group, hyponatremia was seen in 9(27.3%) cases while 16(23.88%) were isonatremic. Out of total 70 male children, 23(69.7%) had hyponatremia while 47(70.25%) were isonatremic and out of total 30 female children, 10(30.3%) had hyponatremia while 20(29.85%) were isonatremic.

Table 3: Hyponatremic Versus Isonatremic Cases In Different Clinical Diagnosis.

Clinical Diagnosis	Hyponatremic (n=33)	Isonatremic (n=67)	Total (n=100)	p-value
Pneumonia	13(25.5%)	38(74.5%)	51(51%)	0.001
Bronchiolitis	8(28.6%)	20(71.4%)	28(28%)	
WALRI	5(35.7%)	9(64.3%)	14(14%)	
Empyema	7(100%)	0	7(7%)	

Difference of clinical diagnosis between hyponatremic v/s isonatremic groups was significant statistically. All cases of empyema had hyponatremia.

Table 4: Association Of Hyponatremia With Hospital Stay & Complications.

Characteristics	Hyponatremic (n=33)	Isonatremic (n=67)	P-value
Hospital stay(day s)	<7	1	27
	>28	14	4
Complications(seizures with altered sensorium)	2(6%)	0	<0.001
Mortality	0	0	-

Children with hyponatremia had longer hospital stay and there was statistically significant difference of hospital stay between hyponatremic v/s isonatremic groups ($p<0.001$). Two cases out of 33 hyponatremic cases had complications in the form of seizures followed by altered sensorium but there was no complication in isonatremic cases. So this difference of occurring of complications in the form of seizures followed by altered sensorium in the hyponatremic versus isonatremic cases was statistically significant ($p= <0.001$) but there was no mortality observed due to hyponatremia in any age group.

DISCUSSION

This was a prospective study with study sample of 100 children in the age group of 2 months to 5 years

admitted with LRI's in children ward at Bebe Nanki Mother and Child Care Center, GMC Amritsar. This observational study was carried out over a time period of one year from January 2017 to January 2018.

In this study 75% children were between 2-12 months and 25% were between 1-5 year of age. There were 70% male children and 30% female children. Although, age and sex had no correlation with hyponatremia in our study comparable to study by Don M et al,^[10] in age and gender but there was male predominance in our study and this gender bias may be due to the reason that male children are brought early to the hospital for treatment than females due to comparatively more preference for male children in our country & other developing countries.

In our study, selected cases were diagnosed on the basis of clinical symptoms and signs & the diagnosis was confirmed radiologically in the same way as is done by Chaitra et al & Clark et al.^[11,12]

In our study hyponatremia was seen in 33(33%) of children admitted with LRI's. This result is comparable with the results of some other studies by Wrotek et al,^[13] in 2013 in their study of 312 it is(33.3%), Massimiliano et al,^[10] in 2001-02 it is (45.4%), Guruswamy et al^[14] in 2014 it is(46.7%) and Sakellaropoulou et al^[15] in 2008-09(35.2%). It was 46.7% in a study by Alkahtani HN et al^[16] in 2016-17.45.4% in a study done in 2001-2002 at Udine, Italy by Don et al & 28% in study in 2008 by Zilberberg et al.^[10,17] In this study the average serum sodium level was $130.19\pm3.37\text{mEq/L}$ in hyponatremic group versus $137.15\pm2.84\text{mEq/L}$ in isonatremic group and it was consistent with results shown by Guruswamy et al,^[14] in 2014. Hyponatraemia in association with LRI's may occur due to many reasons, such as salt deficit, or surplus of water. Other contributory factors may be primary illness, impaired water excretion, improper release of vasopressin, use of hypotonic fluids, redistribution of sodium and water, sick cell syndrome, and numerous drugs.^[15]

All the clinical symptoms were significantly more common as well as of longer duration in the hyponatremic group as compared to isonatremic group similar to a study by Don M et al,^[10] where patients with hyponatremia had higher initial temperature (38.96°C vs 38.45°C , $P=0.008$) in a study done in 2001-02 at DPMSC, Udine, Italy. And also occurrence of clinical signs of respiratory distress were more common in hyponatremic group (HN) as compared to isonatremic group (IN) similar to a study by Sakellaropoulou et al^[15] conducted from January 2008 to May 2009 in 54 children. In our study, diagnosis of study cases was confirmed radiologically similar to other studies like in a study by Chaitra et al^[11] and it was found that abnormal X-ray findings were significantly more common in hyponatremic group than in isonatremic group in

both age groups ($p<0.001$). But Don M et al,^[10] didn't find any association of x-ray finding of consolidation to hyponatremia.

In our study, 26 (26%) patients continued taking normal oral feeds while 74 (74%) patients were given i/v fluids during hospital stay. When this requirement of rehydration fluids was compared in hyponatremic versus isonatremic patients it was found that requirement of i/v fluid in hyponatremic patients was significantly more common than isonatremic patients in both age groups ($p<0.001$). Although no study is available for comparison but as dehydration can occur in bronchiolitis & WALRI patients due to low intake, vomiting in some cases or respiratory losses due to tachypnoea, this aspect should be carefully taken care.

In our study maximum number of hyponatremia was present in pneumonia cases (39.4%) that is consistent with the study by Chaitra et al,^[11] where hyponatremia was present in maximum number in pneumonia cases (46.7%). The association of hyponatremia more with pneumonia in our study also goes with the study by Glatstein et al.^[12] Among 100 children only 7 children had empyema but all empyema cases had hyponatremia. This was consistent with a study by Chaitra et al,^[11] where they found that all cases with empyema had hyponatremia (100%). Hence the study shows that more severe the lung involvement more was the association with hyponatremia.

Fortunately in the majority of cases 17 (51.5%), hyponatremia was mild (S.Na-131-134 meq/l), and in 14(42.5%) cases moderate hyponatremia (S.Na-126-130 meq/l) and only 2(6%) cases had severe hyponatremia (S.Na- \leq 125 meq/l) consistent with the findings of Mandal et al,^[19] who showed mostly mild hyponatremia in 81% cases and severe hyponatremia in 5% cases.

27/33(81.8%) of the children with hyponatremia had low serum osmolality (<280 mOsm/kg), indicating that it is Euvolemic hypotonic hyponatremia. Thus in 27/33 (81.8%) of hyponatremic patients, the most probable cause of hyponatremia was SIADH, as most of the features fit into the criteria of SIADH. Similarly shown in the study by Alkahtani Hassan Nasser et al,^[16] where, 64.3% of the hyponatremia were secondary to SIADH. This observation is similar to the research study done by Prasad et al,^[8] in which 64% of hyponatremia cases was because of SIADH. In another research study done by Singhi et al,^[20] SIADH was the cause in 68% of hyponatremia cases. There are many contributing factors towards the pathogenesis of SIADH in cases of LRI's. Firstly, the stress induced release of ADH causing salt loss and water retention might be reason for hyponatremia.^[21] In addition, severe infections are associated with release of inflammatory mediators like interleukin 6, which stimulates ADH production. Inflammatory markers also stimulates thermoregulatory center resulting in reset of the

thermostat hence the high temperature.^[20,22] Moreover, fever stimulates non-osmotic release of ADH are well explained in the study done by Don M et al.^[10]

The hyponatremic and isonatremic groups were compared for different morbidities related to hyponatremia in children with lower respiratory infections in two age groups, as determined by length of hospital stay and associated complications. It was found that length of hospital stay was significantly ($p<0.001$) longer in children with hyponatremia than in children with isonatremia. It was 49.2% longer in hyponatremic group than in isonatremic group. It was consistent with other studies as, Sakellaropoulou et al,^[15] have also showed in their study in 2008-09 that hyponatremia had 50% longer duration of hospitalization.. In a study by Dhawan et al,^[4] mean duration of hospital stay was about one and half times longer in children with hyponatremia. Thus, hyponatremia contributes to increased morbidity rates by prolonging hospital stay and probably adds to the costs of care.

In our study hyponatremia was associated with increased complications in the form of seizures followed by altered sensorium. 2(6%) cases with hyponatremia found to had seizures followed by altered sensorium but there was no complication in isonatremic cases ($p<0.001$). Singhi and Dhawan reported in their study, hyponatremia to be associated with 60% longer hospital stay,^[2] fold increase in complications compared to that of isonatremia.. It was also consistent with a study done in 2012-13 by Patil J et al,^[23] where hyponatremia with pneumonia was associated with more severe illness, increased mortality risk and extended hospital stay. The occurrence of convulsion and altered sensorium in association with hyponatremia has been explained by different authors. Various studies on hyponatremic an SSs have revealed that hypoxia impairs volume regulation of brain cells, decreases cerebral perfusion, and increases the probability of developing neuronal lesions.^[24] Adaptation of the brain to hyponatremia largely depends on extrusion of sodium from the intracellular space via Na⁺ ATPase pumps. This energy dependent process is impaired in hypoxic conditions. The combination of systemic hypoxia and hyponatremia is more deleterious than in either condition alone, because hypoxia impairs the ability of the brain to adapt to hyponatremia, worsening hyponatremic encephalopathy and thus increasing morbidity.^[25]

CONCLUSION

From the different observations of our study, we conclude that, hyponatremia is a significantly common association among hospitalized children with LRI's in the age group of 2 months to 5 years and it is mainly due to syndrome of inappropriate

antidiuretic hormone secretion (SIADH). Severity of hyponatremia varies with the severity of underlying respiratory pathology. Presence of hyponatremia in LRI's increases the morbidity of these patients in the form of prolonged hospital stay and occurrence of complications like seizures followed by deranged sensorium in some cases. So, such hospitalized children suffering from LRI's should be evaluated for not only clinically but also for serum levels of sodium at the time of admission. Careful fluid management especially in the form of fluid restriction therapy in addition to the specific treatment of the underlying cause can prove very useful in lowering the morbidity and complications in these children.

REFERENCES

- Upadhyay A, Jaber BL, Madias NE. Incidence and prevalence of hyponatremia. *The American journal of medicine*. 2006;119(7):S30-5.
- Eisenhut M. Extrapulmonary manifestations of severe respiratory syncytial virus infection—a systematic review. *Critical Care*. 2006;10(4):R107.
- Hanna S, Tibby SM, Durward A, Murdoch IA. Incidence of hyponatraemia and hyponatraemic seizures in severe respiratory syncytial virus bronchiolitis. *Acta Paediatrica*. 2003;92(4):430-4.
- Dhawan A, Narang A, Singhi S. Hyponatraemia and the inappropriate ADH syndrome in pneumonia. *Annals of tropical paediatrics*. 1992;12(4):455-62.
- Szabo FK, Lomenick JP. Syndrome of inappropriate antidiuretic hormone secretion in an infant with respiratory syncytial virus bronchiolitis. *Clinical pediatrics*. 2008;47(8):840-2.
- Bartter FC, Schwartz WB. The syndrome of inappropriate secretion of antidiuretic hormone. *The American journal of medicine*. 1967;42(5):790-806.
- Halberthal M, Halperin ML, Bohn D. Acute hyponatraemia in children admitted to hospital: retrospective analysis of factors contributing to its development and resolution. *Bmj*. 2001;322(7289):780-2.
- Prasad SV, Singhi S, Chugh KS. Hyponatremia in sick children seeking pediatric emergency care. *Indian pediatrics*. 1994;31:287.
- Gross P. Clinical management of SIADH. *Therapeutic advances in endocrinology and metabolism*. 2012 Apr;3(2):61-73.
- Don M, Valerio G, Korppi M, Canciani M. Hyponatremia in pediatric community-acquired pneumonia. *Pediatric nephrology*. 2008 Dec 1;23(12):2247-53.
- Chaitra KM. Hyponatremia in lower respiratory tract infections. *International Journal of Contemporary Pediatrics*. 2016 Dec 28;3(2):381-4.
- Clark JE, Hammal D, Hampton F, et al. Epidemiology of community-acquired pneumonia in children seen in hospital. *Epidemiol Infect* 2007;135:262e9.
- Wrotek A, Jackowska T. Hyponatremia in children hospitalized due to pneumonia. *Adv Exp Med Biol*. 2013;788:103-8.
- Guruswamy NT, Khan H, Hegde P. Correlation of hyponatremia in children presenting with acute lower respiratory tract infection in a tertiary care hospital. *International Journal of Recent Trends in Science and Technology* October 2014; 12(3):631-4.
- Sakellaropoulou A, Hatzistilianou M, Eboriadou M, Athanasiadou-Piperopoulou F. Hyponatraemia in cases of children with pneumonia. *Archives of medical science: AMS*. 2010 Aug 30;6(4):578.
- Nasser AH, Abdullah AA, Saad AA, Shari AM, Saif AA. Hyponatremia in Children with Acute Lower Respiratory Tract Infections: Overview. *International Journal of Healthcare Sciences*. 2016;4(2):485-9.
- Zilberman MD, Exuzides A, Spalding J. Hyponatremia and hospital outcomes among patients with pneumonia a retrospective cohort study. *BMC Pulmonary Medicine*. 2008;8:16.
- Glatstein M, Rozen R, Scolnik D, Rimon A, Grisaru-Soen G, Freedman S, Reif S. Radiologic predictors of hyponatremia in children hospitalized with community-acquired pneumonia. *Pediatric emergency care*. 2012 Aug 1;28(8):764-6.
- Mandal PP, Garg M, Choudhary IP. To Study the Association and Significance of Hyponatremia in Pneumonia in Paediatric Patients Treated in Hospital Setting. *Age (months)* 2018;5(1):11-14.
- Singhi S. Hyponatremia in hospitalized critically ill children: current concepts. *The Indian Journal of Pediatrics*. 2004 Sep 1;71(9):803-7.
- Poddar U, Singhi S, Ganguli NK, Sialy R. Water electrolyte homeostasis in acute bronchiolitis. *Indian Pediatrics*. 1995;32:59.
- Kaneko K, Kaneko K. Hyponatremia in children with respiratory tract infection. *Pediatr Nephrol*. 2009;24(8):1595.
- PATIL J. Hyponatremia in pneumonia: hospital based cross sectional study. *Journal of Drug Discovery And Therapeutics*. 2015 Jul 24;3(30).
- Halberthal M, Halperin ML, Bohn D. Acute hyponatraemia in children admitted to hospital: retrospective analysis of factors contributing to its development and resolution. *BMJ*. 2001;322(7289):780-2.
- Kennedy PG, Mitchell DM, Hoffbrand BI. Severe hyponatraemia in hospital inpatients. *Br Med J*. 1978;2(6147):1251-3.

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